PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
P22408PC00		
International application No.	International filing date (day/month/year)	Priority date (day/month/year)
PCT/NL99/00460	19/07/1999	22/07/1998

International Patent Classification (IPC) or national classification and IPC
C12N15/31

Applicant
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1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the International application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
22/02/2000	27.10.2000
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Ury, A Telephone No. +49 89 2399 8411

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/NL99/00460

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-80 as originally filed

Claims, No.:

1-29 as originally filed

Drawings, sheets:

1/59-59/59 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 5-6 (totally); 1-3, 7-29 (partially).

because:

Item V.

Reference is made to the following documents:

D1: Elliott et al., J. Hyg. Camb., 1980, 85, pp.275-285
D2: Charland et al., Microbiology, 1998, 144, pp.325-332
D3: Kolkman et al., J. Biochem., 1998, 123, pp.937-45
D: Smith et al., Infection and immunity, April 1999, 67, pp.1750-56.

I) 1) D1 discloses a purified capsular polysaccharide (or antigen) from *Streptococcus suis* type 2 (see summary). This disclosure destroys the novelty (Article 33.2 PCT) of present claim 13.

2) Said purified capsular polysaccharide (or antigen) from *Streptococcus suis* type 2 is used in a vaccine comprising an adjuvant (see also summary). This destroys the novelty (Article 33.2 PCT) of present claim 14.

3) Document D2 discloses two *Streptococcus suis* type 2 mutants having a modified capsular gene cluster. These mutants are obtained by transposon (Tn916) insertion (see summary and "Molecular characterization of mutants", page 327 of D2). This destroy the novelty (Article 33.2 PCT) of present claims 15 and 16.

Note also that claim 16 is anticipated by any naturally occurring *S. suis* since the word "recombinant" does not confer any distinguishing technical feature to a microorganism and the expression "at least a part" encompasses the totality of said capsular gene cluster.

4) Claim 17 being not clear ("A recombinant microorganism... comprising a lactic acid bacterium" implies that other microorganisms are contemplated by the claim), the above objections raised against claim 16 also apply to claim 17.

5) No true technical feature distinguishes "a vaccine comprising a product X" from the product X itself. Following this reasoning, the subject-matter of claims 18-23 also lack novelty under Article 33.2 PCT.

6) Dependent claims 24 and 25 do not appear to contain any additional features which, in combination with the features of any claim to which they refer, meet the requirements of the EPC with respect to inventive step (Article 33.3 PCT).

II) The prior art document D1 discloses the applicability of *S. suis* serotype 2 capsular antigen for vaccination and diagnostic purposes.
In the light of this prior art, a problem underlying the present application can be seen in the provision of further reagents for *S. suis* diagnostic and vaccination purposes. The solution to this problem is the provision of polynucleotides, encoded peptides, and corresponding *S. suis* capsular antigen of serotype 2.

It was known in the art that in Gram-negative bacteria, but also in a number of Gram-positive bacteria, genes which are involved in the biosynthesis of capsule polysaccharides are clustered at a single locus (see the description of the present application page 8, lines 3-8, and D3, page 944, paragraph 2).
The fact that this was also the case for *S. suis* is confirmed by D2 which indicates that "only one transposon insertion is sufficient to alter capsular expression" (page 327, last sentence of "Molecular characterization of mutants).
Furthermore, D2 discloses 2 mutants having Tn916 insertions in the capsular gene cluster of *S. suis* type 2. This allows the identification and isolation of the gene cluster containing said transposon.
Thus, starting from this prior art the provision of polynucleotides, encoded peptides, and corresponding *S. suis* capsular antigen of serotype 2 would have been routine for the skilled person by use of classical technics in the field of molecular biology. At least the skilled person would have had a reasonable expectation of success.
Therefore, the subject-matter of present claims 1-14 lack an inventive step under Article 33.3 PCT.

III) It seems that the use of a *S. suis* type 2 mutant deficient in capsular expression as a vaccine was not derivable in an obvious manner from the available prior art.
Therefore, the subject matter of present claim 26 (except when this claim refers back to claim 18) and claims 27-29 fulfil the requirements of Article 33.3 PCT.

IV) It appears that almost half of the nucleic acid encoding the capsular gene cluster

(CPS2) depicted in Fig.3 is lacking in the priority documents of the present application. Thus, the sequence of Fig.3 (or at least a part of it) does not enjoy the priority right, and document D becomes highly relevant with respect to the subject-matter corresponding to Fig.3.

V) For the assessment of the present claim 26 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Item VIII.

1) It is clear from the description that the nucleic acid sequence(s) of Fig.3 is an essential technical feature to the definition of the invention.
Since none of the independent claims contain this feature (note that the word "preferably" in claim 4 renders this feature optional) they do not meet the requirement following from Article 6 PCT taken in combination with Rule 6.3(b) PCT that any independent claim must contain all the technical features essential to the definition of the invention.

2) One subject in a population partly vaccinated can be a subject which has not been vaccinated at all. Thus, the subject-matter of claims 27 and 28 encompasses embodiments which do not have the technical features of the invention (Article 6 PCT).

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/NL99/00460

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 5-6 (totally); 1-3, 7-29 (partially).

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 1-4, 7-12, 24-29
	No:	Claims 13-23
Inventive step (IS)	Yes:	Claims 26-29
	No:	Claims 1-4, 7-25
Industrial applicability (IA)	Yes:	Claims 1-4, 7-25, 27-29
	No:	Claims

2. Citations and explanations

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet